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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,530	09/05/2003	Peter Distefano	13407-020001	9529

26161 7590 09/24/2007

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EXAMINER
LIU, SUE XU

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
09/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/656,530	DISTEFANO ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30,32-34 and 36* is/are pending in the application.

4a) Of the above claim(s) *1-24 and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-30 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Claim Status

Claims 31 and 35 have been cancelled as filed on 7/3/07.

Claims 1-30, 32-34 and 36 are currently pending.

Claims 1-24 and 32-34 have been withdrawn.

Claims 25-30 and 36 are being examined in this application.

Election/Restrictions

1. Applicant's election of Group VI (Claims 25-31) without traverse in the reply filed on 10/11/06 is as previously acknowledged.

2. Applicant's election with traverse of the following species in the reply filed on 10/11/06 is as previously acknowledged:

A.) Ghrelin receptor as the GH/IGF-1 axis component;

B.) A non-human animal model to be contacted by a compound;

C.) A small organic molecule as the test compound;

D.) A metabolic disorder as a disorder;

E.) A cell surface receptor;

F.) The species requirement of "A single specific and defined number of nucleotide mutations per nucleic acid sequence" as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

G.) An antagonist;

H.) A cell-based assay;

I.) A human subject as a subject;

J.) The species requirement of "A single selection of an age-associated parameter" as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

K.) The species requirement of "A single selection of a direct antagonist…" as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

Specification

3. Applicant's amendment to the specification to correct the recitation of "FIG. 1" on page 39 is acknowledged.

Sequence Rule Compliance

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) below:

Applicants are respectively directed to the attached "Notice to Comply" for further details on compliance with the Sequence Rule. Applicants are requested to submit sequence listings and amend the instant specification accordingly.

Priority

5. This application claims priority to the following U.S. Provisional Patent Application Nos. 60/487,308, filed on 7/14/2003, 60/487,344, filed on 07/14/2003, and 60/408,560, filed on 09/06/2002.

Claim Rejections Withdrawn

6. In light of applicants' amendments to the claims and supporting arguments, the following claim rejections as set forth in the previous office action are withdrawn:

A.) Claims 25-30 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

B.) Claims 25-30 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

(Note: the instant claim numbers are in bold font.)

Smith

8. Claims 25-30 and 36 are rejected under **35 U.S.C. 102(b)** as being anticipated by Smith et al (Endocrine Reviews. Vol. 18(5): 621-645; Oct., 1997; cited previously). This rejection is maintained for the reasons of record as well as the discussion below. The rejection over claim 31 is moot due to applicant's cancellation of said claim.

Smith et al, throughout the publication, teach various compounds (peptidomimetics) that can be used for regulation of growth hormone (GH) secretion (see entire document). The reference teaches various compounds (peptides or peptidomimetics) that can modulate activities of at least the GH and GHSR (Ghrelin receptor) in the GH/IGF-1 axis (pp. 621-627; especially, p. 624. right col., p. 625, left col., and p. 630, right col.). The MK-0677 (p. 625, Figure 4), for example, reads on the test compound of the claimed test compound of **clm 25**. The MK-0677 is a derivative of an antagonist or an agonist (p. 624, right col., para 2 and p. 625, left col., para 2), which reads on the chemically modifying an agonist of the GH/IGF-I component of **clm 25**. The reference also teaches pituitary cell based assay, and GH hormone assay in rats and dogs (p. 625, Left-right col., bridging para), which reads on step b) of **clm 25**, and cell-based assay of **clms 26 and 27**. The reference specifically teaches that the beagles has elevated GH and IGF-I levels after administering MK-0677 (p. 625, left-right col., bridging lines), and thus the beagles has normal IGF-1 levels prior to administering as recited in **clm 28**. The reference's teaching (p. 625, Left-right col., bridging para) also reads on a cohort of adult animals as recited in **clm 29**, and the evaluating step of **clm 31**. The reference teaches administering oral dosage to dogs or rats (p. 625, left col., para 2, p. 635, left-right cols.), which reads on the pharmaceutically acceptable carrier of **clm 36**. The reference also teaches particular dosing regimens of MK-0677 for dogs

lowered IGF-I to basal levels (p. 635, right col.) and lowered GH level to basal levels as well (p. 636, left col., para 1), which reads on the decreased levels of GH and/or IGF-1 of **clm 30**.

Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the Smith reference teaches "amplification of the GH-secretory patway", and thus the Smith reference does not teach an "antagonist". (Reply, p.13).

Applicants are respectively directed to the previous Office action as well as the discussion above for detailed analysis of the Smith reference. The Smith reference teaches administering Mk-0677 and observed a decrease in GH and IGF-1 (the underlined region in the above discussion), which reads on the instant claim 30.

New Claim Rejection(s)

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Blum

11. Claims 25, 26 and 36 are rejected under **35 U.S.C. 102(b)** as being anticipated by Blum et al (Biochemistry. Vol. 39: 15705-15712; 2000; cited in IDS). This rejection is necessitated by applicant's amendment to the claims.

Blum et al, throughout the publication, teach using inhibitor to inhibit IGF-1 receptor (Abstract). The reference teaches using various inhibitors such as I-OMe AG 538 for inhibition of IGF-1R (e.g. p.15707, right col. para 6; Table 1), and chemical synthesis of the inhibitor (e.g. p.15706, col.1, para 3), which read on step a) of **clm 25**. The reference also teaches incubating the inhibitors with cells for testing the inhibitors abilities to inhibit (or antagonize) IGF-1R in both cell and cell free systems (e.g. p.15709; p.15706), which read on step b) of **clm 25** and **clm 26**.

The reference also teaches using various buffers or solutions for incubation of the inhibitors with cells (e.g. p.15706, col.2, para 2 and 4), which the solutions and buffers read on pharmaceutically acceptable carrier of **clm 36**.

Deghenghi

12. Claims 25-27, 30 and 36 are rejected under **35 U.S.C. 102(b)** as being anticipated by Deghenghi et al US 5,962,409; cited in IDS). This rejection is necessitated by applicant's amendment to the claims.

Deghenghi et al, throughout the publication, teach using peptides for inhibition of growth hormone (GH) secretion (Abstract). The reference teaches various peptides that inhibit the release of GH (e.g. cols.1-2). The reference also teaches synthesis of cyclic peptides (e.g. col.2, lines 1+; col.3, lines 1+), which read on step a) of **clm 25**.

The reference also teaches incubating the peptides to animal and human cells to test the effect of the compound on GH release (e.g. col. 4, lines 28+), which read on step b) of **clm 25**, and cell system of **clm 26**.

The reference also teaches administering the peptides to animals and humans (e.g. col.3, lines 65+; Claims 4 and 8), which read on the step of **clm 27**. The reference also teaches measuring the GH level (e.g. col.6, lines 5+), which reads on the limitation of **clm 30**.

The reference also teaches using various buffers or solutions for incubation of the inhibitors with cells (e.g. col.5, lines 10+; claim 4), which the solutions and buffers read on pharmaceutically acceptable carrier of **clm 36**.

Orrego

13. Claims 25-30 and 36 are rejected under **35 U.S.C. 102(a)** as being anticipated by Orrego et al (Journal of Clinical Endocrinology and Metabolism. Vol. 86(11): 5485-5490; cited in IDS). This rejection is necessitated by applicant's amendment to the claims.

Orrego et al, throughout the publication, teach using an antagonist of GHRH-R to reduce GH in human (Abstract). The reference teaches administering a GHRH antagonist to human such as (N-Ac-Tyr1, D-Arg2)GHRH-(1-29)-NH2) or GH-44, which compounds are modification of the GHRH (an "agonist"). (e.g. p.5486, col.1, para 1; Figure 1; Figures 2-4). The GHRH antagonists read on the antagonist obtained from an agonist of **clm 25**, and the administering reads on the steps of **clm 25**.

The reference also teaches various assays for measuring GH levels (e.g. p.5486, left col., para 3), which reads on the cell free assay of **clm 26**.

The reference teaches administering the compounds to adult humans (e.g. Table 1), which reads on the limitation of **clm 27**.

The reference also teaches the adult humans have normal IGF-1 levels (e.g. Table 2; p. 5485, right col.), which reads on the limitations of **clms 28, 29** and **30**.

The reference also teaches administering the antagonists as boluses (e.g. Figure 1; p.5486, left col., para 1), which read on the pharmaceutical carrier of **clm 36**.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
9/5/07

MARK L. SHIBUYA
PRIMARY EXAMINER

Notice to Comply	Application No. 10656530	Applicant(s) DISTEFANO ET AL.	
	Examiner Sue Liu	Art Unit 1639	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The instant specification recites amino acid sequences (e.g. p.53), which are not identified by their corresponding SEQ ID NOs. The specification has not been checked to the extent necessary to determine the presence of all possible recitation of sequences. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

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Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: markspencer

Timestamp: Fri Jul 13 10:27:59 EDT 2007

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Reviewer Comments:

There is a "1" after the last sequence at the end of the file. Please remove this extra material.

****

Validated By CRFValidator v 1.0.2

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Actual SeqID Count: 3

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Bayley, Cynthia A.
Cannon, L. Edward

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